definitive RT/CT. Further treatment intensification for patients with relative SUV >0.57 seems justified.

PO-0671

Is the GTV a better prognostic factor for the OS for patients treated with CCRT for locally advanced NSCLC than the PTV?

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Purpose/Objective:

Introduction: In literature a lower survival in a larger GTV was found in a retrospective analysis of a prospective database of 270 patients (Dehing-Oberije). These patients were treated with (chemo) radiotherapy for NSCLC. This raises the question to specify the GTV and the PTV further with a cutoff point in our own database with patients treated with CCRT for locally advanced NSCLC.

Purpose: Is the GTV a better predictor of outcome of treatment (LC, LRC, DFS, OS) than the PTV? Can we find a cut-off with the inclusion of the volume prediction (GTV or PTV) to use the least toxic treatment with the same or better result for patients with locally advanced non-small cell lung carcinoma (NSCLC)?

Materials and Methods: In 132 patients (PET-CT staged) treated with CCRT for locally advanced non-small cell lung carcinoma in the period 2005-2012, one observer delineated the GTV of the primary tumor and lymph nodes and the volume (cc) was calculated. The planning target volume (PTV) was generated, prognostic factors and outcome registered retrospectively. The Cox regression model and multivariate support will be calculated and the difference will be tested. The median volume (GTV and PTV) cutoff applied and tested separately for consistency in the spline predict model.

Results: In the univariate analysis GTV (>77 cc) (p=0,031/HR 1.9), PTV (>390 cc) (p=0.0035/HR 2,4) and gender (p<0,001/HR 0.3) are significantly favorable prognostic factors for overall survival (OS). In the multivariate cox-regression analysis PTV >390 cc (p=0.012/HR 2,5) and gender (p=0,006/HR 0.35) (male: female) but not GTV are significantly favorable prognostic factors for OS. Age is in the univariate analysis (p=0.018/HR 0.96) and multivariate analysis (p=0.01/HR 0.95) the only significantly favorable prognostic factor for local relapse free survival.

Conclusions: The GTV does not have a better prognostic value for overall survival and local recurrence free survival in patients with locally advanced NSCLC treated with CCRT than the PTV (Correlation factor =0.94).

A cut off point for overall survival was found for GTV 77 cc and PTV 390 cc.

Reference:

Dehing-Oberije C, De Ruysscher D, van der Weide H, et al. Tumor volume combined with number of positive lymph node stations is a more important prognostic factor than TNM stage for survival of non-small-cell lung cancer patients treated with (chemo) radiotherapy. Int J Radiat Oncol Biol Phys 2008; 80(4): 1039-1044

PO-0672

Predicting tumor control from dose and fractionation schedule: fitting and validation with clinical data

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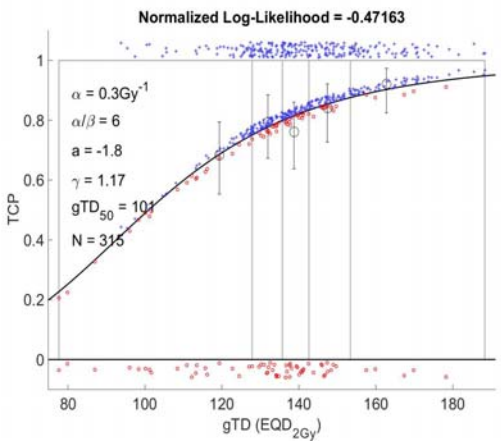
Purpose/Objective: When formulating radiation treatment plans, it has long been assumed that tumor doses should be kept homogeneous throughout the tumor in order to maximize the likelihood of tumor control. This has lead to the widespread adoption of 'D_{95}' as the standard plan-quality metric. However, the optimization of this parameter is often achieved at the expense of competing dose-volume metrics, putting the patient at increased risk of normal tissue toxicities despite scant clinical data to support the need for dose homogeneity, and mounting biological evidence against it. With this in mind, we set out to derive a novel, mechanistically-derived metric which accurately derives tumor control probabilities from each patient's unique dose distributions and fractionation schedules: 'generalized tumor dose' (gTD).

Materials and Methods: The gTD metric was inspired by Niemierko's concept of gEUD, which applies a generalized-mean term ('a') to the dose distribution over the structure of interest. Here we apply the same concept, however incorporating it into a dose-effect model mechanistically derived from known tumor radiobiology, and accounting for each patient's unique dosing, fractionation schedule, and tumor characteristics. In effect, the derived gTD metric reflects the level of absolute cell survival within the tumor, subject to the 'a'-based relative weighting of the high or low end of the dose distribution. Using parameter optimization methods on clinical lung tumor data from two institutional cohorts (NKI: N=266 & WUSTL: N=50), we tested the current assumption that outcome (local control/failure at last followup) is determined by the sum of independent dose effects to tumor sub-volumes.

Results:



Fitting model parameters to the combined cohort data using both log-likelihood and actuarial methods, we were able to

derive optimized α and α /ß of 0.3Gy^{-1} and 6Gy, respectively. We also found a generalized mean value of a=-1.7 (95% confidence interval upper bound=-0.1), which produces the best performing gTD predictive metric (Fig.).

Conclusions: A negative 'a' value suggest that areas of low cell survival (high dose) play a driving role in determining whether local control is achieved, regardless of dose homogeneity. In this first known case of multi-institutional investigation of case-specific treatment effects, we demonstrated the utility and superior predictive power of this novel, biologically-inspired dose-metric.

PO-0673

Stereotactic body radiotherapy for histopathologically confirmed vs. presumed early stage NSCLC

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Purpose/Objective: Medically inoperable early stage non-small cell lung cancer (NSCLC) is frequently treated with stereotactic body radiotherapy (SBRT). As this patient population is often frail, not only is surgery a potential morbid procedure, but obtaining a pathologic diagnosis of cancer may be risky as well. It is becoming more common to treat patients empirically with growing, positron emission tomography (PET) avid lung nodules with SBRT. This study looked to compare outcomes between patients with a histopathologic diagnosis of cancer compared to patients without a diagnosis.

Materials and Methods: A retrospective review of patients enrolled on a prospective IRB-approved registry from 2004 to 2013 was conducted. Patients with a non-diagnostic biopsy or no attempted biopsy were considered to lack a histopathologic diagnosis. Patients with synchronous cancers or prior invasive malignancy within 2 years of SBRT were excluded. Kaplan-Meier curves for local control (LC), progression-free survival (PFS), recurrence-free survival (RFS), and overall survival (OS) were created by Wilcoxon analysis. Patients were evaluated for risk factors predicting for LC, PFS, RFS, and OS using Cox regression.

Results: A total of 427 patients were included in the analysis. Median age was 74 years old with a median follow-up of 17 months (range, 0.2 to 105 months). Of all patients, 332 (78%) underwent biopsy confirming diagnosis of malignancy, with 124 (37%) patients with adenocarcinoma, 98 (30%) patients with squamous cell, 98 (30%) patients with NSCLC not otherwise specified, and 12 (4%) patients with other histologies. Ninety-five patients (22%) were treated empirically for suspected lung cancer, of which 92 (97%) were staged with PET/CT. Patients treated without a diagnosis were more likely to have a prior history of cancer, smaller tumors, lower BMI, and a lower PET standardized uptake value maximum compared with patients with a diagnosis. There was no difference between the groups at baseline with regard to age, race, gender, smoking status, Charlson comorbidity score, KPS, central location, use of mediastinal staging, or use of PET/CT staging. For the entire cohort, 2 year LC, PFS, RFS and OS was 91%, 47%, 64% and 61%, respectively. There was no difference in LC, PFS, RFS, and OS between patients with and without biopsy. On multivariate analysis, factors predictive for improved OS included KPS ≥70 {hazard ratio (HR) 0.552 [95% confidence interval (CI), 0.383-0.796, p=0.005]}, larger CT size of tumor [HR 1.195 (95% CI, 1.033-1.383), p=0.003] and post-treatment CT scan showing partial or complete response [HR 0.399 (95% CI, 0.164-0.968, p=0.012)].

Conclusions: In carefully selected patients without a biopsy, SBRT results in comparable survival and tumor control compared with patients treated with a biopsy.

PO-0674

Brain relapses in stage III NSCLC after multimodality treatment: prognostic factors from a randomised trial

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Purpose/Objective: To identify prognostic factors for brain relapses. A secondary analysis of a prospective randomized trial of definitive radiochemotherapy (RT/CT) compared with neoadjuvant RT/CT+surgery was performed.

Materials and Methods: Pts with pathologically proven operable IIIA(N2) / selected IIIB NSCLC received 3 cycles cisplatin/paclitaxel and neoadjuvant chemoradiotherapy to 45 Gy (1.5 Gy bid/ concurrent cisplatin/ vinorelbine). Pts were reevaluated within an interdisciplinary panel during last week of RT/CT. Operable pts were randomized either to definitive RT/CT (arm A: risk- adapted boost to 65/71 Gy at 2 Gy per fraction without break and concurrent cisplatin/vinorelbine) or surgery (arm B). Depending on institutional policy, PCI could be applied after completion of chemotherapy.

Results: Between 1/2004 and 8/2012, 246 pts (70 F/176 M; stages, 75 T1-3 N2 / 80 T4 N0-1/ 91 T4 N2 or T1-3N3; histology, 95 SCC / 107 ADC / 44 other) were enrolled from 5 centers, 161 patients were randomised (arm A: 80 pts, arm B:81 pts). Brain relapse as part of any relapse was observed in 33 randomised pts, isolated brain failures were detected in 23 pts. Freedom from isolated brain relapse (FFIBR) at 2 years was 84 (78-90)% for all patients, arm A 83 (73-93)%, arm B 81 (71-91)%. 42 pts recieved prophylactic cranial irradiation. PCI did not influence the incidence of isolated brain relapses (FFIBR at 2 years with or without PCI: 84 (70-98)% vs 81 (73-89)%, p=0.93). Factors associated with a higher incidence of isolated brain relapses in univariate analysis were female gender (FFIBR at 2 years: 89 (81-97)% (male) vs 72 (58-86)%, p=0.03) and TN-stage subgroup (FFIBR at 2